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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/785,230	02/25/2004	Tadamitsu Kishimoto	046124-5042-01	1453

9629 7590 08/30/2005

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EXAMINER	
NICKOL, GARY B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 08/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/785,230	KISHIMOTO ET AL.	
	Examiner	Art Unit	
	Gary B. Nickol Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-27 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-27 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-23, and 25-30 are pending.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-5, 9, 11, 13, as specifically drawn to a therapeutic agent that *inhibits SDF-1* in an antagonistic competition with CXCR4 wherein said agent is a SDF-1-like polypeptide, a variant or fusion thereof, or a structure similar to a binding site of SDF-1, classified in class 530, subclass 350.

II. Claims 1-5, 9, 12, and (14, in part), as specifically drawn to a substance that *inhibits SDF-1* wherein the substance inhibits SDF-1 from binding to CXCR4 by binding to SDF-1, wherein said substance is an anti- SDF-1 antibody or fragment thereof, classified in class 530, subclass 387.1.

III. Claims 1-5, 9, 12, and (14, in part), as specifically drawn a substance that *inhibits SDF-1* wherein the substance inhibits SDF-1 from binding to CXCR4 by binding to SDF-1, wherein said substance is "a fused protein possessing binding activity to SDF-1", classified in class 424, subclass 192.1.

IV. Claims 1-5, 9, 12, and 14 (in part), as specifically drawn to a substance that *inhibits SDF-1* wherein the substance inhibits SDF-1 from binding to CXCR4 by binding to SDF-1, wherein said substance is "substance that induces a structural change in SDF-1", classified in class 514, subclass 1.

V. Claims 1-5, 9, 12, and 14 (in part), as specifically drawn to a substance that *inhibits SDF-1* wherein the substance inhibits SDF-1 from binding to CXCR4 by binding to SDF-1, wherein said substance is "a low molecular weight compound capable of binding to the CXCR-4-binding site of SDF-1", classified in class 514, subclass 1.

VI. Claims 1-5, 10, 15, and (17, in part) as specifically drawn to a therapeutic substance that *inhibits CXCR4* wherein the substance inhibits CXCR4 in antagonistic competition with CXCR4 for binding to SDF-1 wherein said substance is soluble CXCR4 or a variant, or fusion peptide thereof, classified in class 530, subclass 350.

VII. Claims 1-5, 10, 15, and (17, in part) as specifically drawn to a therapeutic substance that *inhibits CXCR4* wherein the substance inhibits CXCR4 in antagonistic competition with CXCR4 for binding to SDF-1 wherein said substance is "a low molecular weight compound having a structure similar to a binding site of SDF-1", classified in class 530, subclass 300.

VIII. Claims 1-5, 10, 16, and (18, in part) as specifically drawn to a therapeutic substance that *inhibits CXCR4* wherein the substance inhibits SDF-1 from binding to CXCR4 by binding to CXCR4 wherein said substance is an anti-CXCR4 antibody or a fragment thereof, classified in class 530, subclass 387.1.

IX. Claims 1-5, 10, 16, and (18, in part) as specifically drawn to a therapeutic substance that *inhibits CXCR4* wherein the substance inhibits SDF-1 from binding to CXCR4 by binding to CXCR4 wherein said substance is a fused protein possessing binding activity to CXCR4, classified in class 424, subclass 192.1.

X. Claims 1-5, 10, 16, and (18, in part) as specifically drawn to a therapeutic substance that *inhibits CXCR4* wherein the substance inhibits SDF-1 from binding to CXCR4 by binding to CXCR4 wherein said substance "induces a structural change in SDF-1", classified in class 514, subclass 1.

XI. Claims 1-5, 10, 16, and (18, in part) as specifically drawn to a therapeutic substance that *inhibits CXCR4* wherein the substance inhibits SDF-1 from binding to CXCR4 by binding to CXCR4 wherein said substance is "a low molecular weight compound capable of binding to the SDF-1-binding site of CXCR4", classified in class 514, subclass 1.

XII. Claims 1-4, 6, and (19, in part) as specifically drawn to a therapeutic agent that inhibits signaling from CXCR4 to nuclei wherein the substance inhibits a MAPK cascade inhibitor, classified in class 514, subclass 1.

XIII. Claims 1-4, 6, and (19, in part) as specifically drawn to a therapeutic agent that inhibits signaling from CXCR4 to nuclei wherein the substance inhibits a "phospholipase C inhibitor", classified in class 514, subclass 1.

XIV. Claims 1-4, 6, and (19, in part) as specifically drawn to a therapeutic agent that inhibits signaling from CXCR4 to nuclei wherein the substance inhibits a "PI3 kinase inhibitor", classified in class 514, subclass 1.

XV. Claims 1-4, 7, 20, as specifically drawn to a therapeutic agent that inhibits the expression of CXCR4 wherein said substance causes the disappearance of CXCR4 by acting on a cell membrane to vary fluidity, classified in class 514, subclass 1.

XVI. Claims 1-4, 7, 21, as specifically drawn to a therapeutic agent that inhibits the expression of CXCR4 wherein said substance is selected from the group consisting of an antigene, an antisense polynucleotide, an antisense RNA expressed by an antisense vector, a ribozyme, and an inhibitor against the expression control site of CXCR4, classified in class 536, subclass 24.5.

XVII. Claims 1-4, 8, 22-23, as specifically drawn to a therapeutic agent that inhibits the expression of SDF-1 wherein said substance is an antisense polynucleotide that inhibits expression of SDF-1 or wherein said substance inhibits the expression control site of SDF-1, classified in class 536, subclass 24.5.

XVIII. Claims 25-26, 28 drawn to a method for treating a solid tumor or suppressing neovascularization comprising administering a substance that inhibits binding between the ligand SDF-1 and the receptor CXCR4, classified in class 514, subclass 44.

XIX. Claims 25-26, 29 drawn to a method for treating a solid tumor or suppressing neovascularization comprising administering a substance that inhibits signaling from CXCR4 to nuclei, classified in class 514, subclass 44.

XX. Claims 25-26, 30 drawn to a method for treating a solid tumor or suppressing neovascularization comprising administering a substance that inhibits the expression of SDF-1, classified in class 514, subclass 44.

XXI. Claim 27, drawn to a method for repairing a tissue comprising administering a substance that inhibits the action due to CXCR4, classified in class 514, subclass 1.

The inventions are distinct, each from the other because of the following reasons:

The Inventions of Groups I-XVII all encompass various inhibitors that broadly encompass different biological structures, different physiological functions, and different modes of operation. For example, some of the inhibitors specifically inhibit the distinct ligand, SDF-1, while some of the inhibitors specifically inhibit the receptor, CXCR4. Further, the majority of the inhibitors are mechanistically distinct. For example, Inventions XII-XIV comprise agents that inhibit cellular signaling while inventions XV-XVII target the expression of CXCR4 or SDF-1. In each case, the inhibitors themselves are unrelated, and structurally distinct molecules. For example, an antisense molecule targeting the expression of SDF-1 is chemically distinct from an antisense molecule that targets the expression of CXCR4 in that each molecule comprises distinct nucleic acid molecules. Further, each product can be made by materially different methods and used in materially different methods. For example, Groups II-V are all drawn to inhibitors with similar functions in that they inhibit SDF-1. However, the inhibitor product of Group II (antibodies) differs structurally and functionally from the inhibitor products of Groups III-V. Further, even though the inventions of Group II and Group III are composed of amino acids (i.e. antibodies vs. fusion peptides), they are structurally dissimilar. The polypeptides of Group III encompass single chain molecules, whereas the polypeptides of Group II encompass antibodies. This would include IgG which comprises 2 heavy and 2 light chains containing constant and variable regions, and framework regions which act as a scaffold for the 6 complementarily determining regions (CDR) that function to bind an epitope. Thus, the

polypeptide of Group III and the antibody of Group II are structurally distinct molecules. Any relationship between the fused polypeptides of Group III and an antibody of Group II is dependent upon the correlation between the scope of the polypeptides that the antibody binds and the scope of the antibodies that would be generated upon immunization with the polypeptide. Further, the antibodies, peptides, fusion peptides, polynucleotides (antisense), anti-signaling molecules, and low molecular weight compounds of the various inventions have a separate status in the art as shown by their different classifications that would require different searches in the literature.

The inventions of Groups XVIII-XXI are materially distinct methods that differ at least in objectives, method steps, reagents and/or dosages and/or schedules used, response variables, and criteria for success. This includes methods for treating a solid tumor or suppressing neovascularization comprising administering a substance that inhibits binding between the ligand SDF-1 and the receptor CXCR4, methods for treating a solid tumor or suppressing neovascularization comprising administering a substance that inhibits signaling from CXCR4 to nuclei, methods for treating a solid tumor or suppressing neovascularization comprising administering a substance that inhibits the expression of SDF-1, or methods for repairing a tissue comprising administering a substance that inhibits the action due to CXCR4.

Hence, the methods differ in their objectives, response variables, and criteria for success.

The inventions of Groups I-XVII and the methods of Groups XVII-XX are related as products and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (I) the process for using the product as claimed can be practiced with

another materially different product or (ii) the product as claimed can be used in a materially different process of using that product [see *MPEP* § **806.05(h)**]. In the instant case the products, as claimed, can be used in materially different processes such as methods of treating a solid tumor, or methods of repairing a tissue.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper. Furthermore, because these inventions are distinct for the reasons given above and the search required for one group is not required for another group, restriction for examination purposes as indicated is proper.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper. Furthermore, because these inventions are distinct for the reasons given above and the search required for one group is not required for another group, restriction for examination purposes as indicated is proper.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Note:

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. Process claims that depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

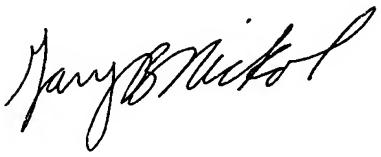
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 571-272-0835. The examiner can normally be reached on M-Th, 8:30-5:30; alternate Fri., 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary B. Nickol Ph.D.
Primary Examiner
Art Unit 1642

GBN



GARY B. NICKOL, PH.D.
PRIMARY EXAMINER